Commentary

The case for improving the detection and treatment of obstructive sleep apnea following stroke

Mark I. Boulos MD MSc

■ Cite as: *CMAJ* 2023 March 13;195:E374-5. doi: 10.1503/cmaj.230240

See related research at www.cmaj.ca/lookup/doi/10.1503/cmaj.221063

Stroke is a leading cause of death and disability for people in Canada. Beyond the initial brain injury, the sequelae of stroke may also include several comorbidities, with sleep disorders being among the most important. Obstructive sleep apnea (OSA) and sleep–wake disturbances are highly prevalent among patients who have had a stroke; they may be both a risk factor for and a consequence of stroke, and can substantially affect stroke recovery and functional outcomes.[1] Moreover, post-stroke fatigue is a top research priority for patients who have had a stroke.[2]

In related research, Jeffers and colleagues[3] used cross-sectional data from the Canadian Community Health Survey to study relative rates of 4 self-reported sleep disturbances, namely having trouble staying awake, either short (< 5 h) or long (> 9 h) nightly sleep duration, having trouble going to or staying asleep, and having unrefreshing sleep. Almost two-thirds of respondents who reported a history of stroke also reported sleep difficulties; those with a history of stroke also reported each form of sleep disturbance significantly more frequently than those without a history a stroke.

Although the authors of the related research did not specifically examine OSA, many of the sleep concerns among those who reported a history of stroke were likely driven by OSA, the most common post-stroke sleep disorder, which has been reported to occur in as many as 72% of patients who have had a stroke or transient ischemic attack (TIA), depending on OSA severity.[4] Patients with pre-existing OSA have poorer functional outcomes and spend more time in rehabilitation after a stroke.[5] Randomized controlled trials have shown that treatment of post-stroke OSA using continuous positive airway pressure (CPAP) improves neurologic recovery and quality of life, and reduces daytime sleepiness and depressive symptoms.[6,7]

Given that OSA is a well-established risk factor for stroke, with a greater adjusted relative risk for stroke similar to or higher than traditional modifiable vascular risk factors that are commonly managed after stroke,[8] it would make sense that OSA be routinely screened for and treated after stroke. However, a 2019 study suggested otherwise.[9]

Key points

- Obstructive sleep apnea (OSA) is prevalent and harmful after stroke.
- Investigation of sleep disorders, particularly OSA, should be strongly considered for patients who have had a stroke, with the goal of improving nonvascular outcomes.
- Obstructive sleep apnea should be treated like a vascular risk factor.
- Future trials will assess whether treatment for OSA initiated early after stroke reduces stroke recurrence.

Lack of screening for OSA after stroke may be explained by several barriers. Obstructive sleep apnea often presents atypically after stroke, and many patients with OSA who have had a stroke do not have the typical clinical features of OSA, such as obesity and daytime sleepiness.[10] Many clinicians may be unaware of the importance of managing OSA and any associated symptoms after stroke. Moreover, testing for sleep disorders requires a multidisciplinary approach, and stroke rehabilitation centres may not have the necessary expertise to conduct sleep testing. Furthermore, the current gold standard for diagnosing OSA, in-laboratory sleep testing or polysomnography, is inconvenient for patients who are vulnerable and those with disabilities, and access to such testing in some Canadian centres may be limited. In a randomized controlled trial that assigned 250 consecutively recruited patients with a history of stroke or TIA to either ambulatory or in-laboratory sleep testing, rates of OSA diagnosis and treatment, as well as functional outcomes and daytime sleepiness, were significantly improved in the ambulatory testing arm.[11] These results suggest that removing the barriers associated with in-laboratory sleep testing (through the use of ambulatory testing for OSA) may enhance outcomes among patients who have had a stroke or TIA.

Finally, screening for and management of OSA after stroke is underemphasized in stroke guidelines. For example, the 2014 and 2018 guidelines from the American Heart Association and the

American Stroke Association for the secondary prevention of stroke stated that evaluation for OSA "may be considered" for patients with stroke or TIA.[12] The most recent version of the Canadian Stroke Best Practice Recommendations removed recommendations on management of sleep apnea,[13] although earlier versions did comment on OSA.

Fundamental to the question of whether clinicians should screen for and manage OSA after TIA or stroke is whether treatment of OSA after stroke or TIA reduces incident vascular events or mortality. Although studies assessing the impact of CPAP on nonvascular outcomes among patients with post-stroke OSA have shown positive outcomes, trials evaluating whether CPAP can reduce the risk of incident stroke or death have been largely negative.[6] The largest of these trials, the Sleep Apnea Cardiovascular Endpoints (SAVE) trial,[7] randomized 2717 patients with coronary or cerebrovascular disease (including 1432 with ischemic stroke or intracerebral hemorrhage) to receive CPAP or usual care. Although the overall findings showed no significant reduction in risk of vascular events or death, a preplanned post hoc subgroup analysis showed that patients who had good adherence to CPAP had a significantly lower risk of cerebrovascular events than those in the usual care group. This was consistent with the findings of earlier, smaller trials that also showed that significant reductions in incident vascular events occurred in subgroups with good CPAP adherence.[14,15] Since randomization was not respected in these subgroup analyses, the findings should be interpreted with caution.

It is important to note that the evidence for various interventions in stroke care has varied over time. Evidence related to OSA is rapidly evolving, and future trials that look at outcomes related to OSA after stroke will need to reconsider how OSA is defined and consider selecting patients on the basis of distinct clinical phenotypes.[16,17] For patients who cannot tolerate CPAP, many new treatment alternatives — including use of pharmacological agents, hypoglossal nerve stimulation, oropharyngeal exercises and dental appliances — have been shown to be effective outside of the stroke population; these need to be evaluated for patients who have had a stroke or TIA.[18] Reflecting what has been seen in other studies evaluating secondary stroke prevention strategies (e.g., antiplatelet trials), interventions for OSA will need to be administered in the hours and days after stroke and not in a delayed fashion, as was done in the SAVE trial. Furthermore, in future trials, sample sizes and follow-up periods need to be carefully calculated to assure adequate power and outcome assessment.[6]

Investigation of sleep disorders, particularly OSA, should be strongly considered for patients who have had a stroke, with the goal of improving nonvascular outcomes, such as daytime sleepiness, mood and functional outcomes. A good argument can be made for treating OSA like any other vascular risk factor.[8] Future trials, such as the ongoing Sleep for Stroke Management and Recovery Trial (Sleep SMART Trial; NCT03812653), will assess whether CPAP treatment for OSA that is started early after stroke reduces stroke recurrence.

References

1. Hermann DM, Bassetti CL. Role of sleep-disordered breathing and sleep-wake disturbances for stroke and stroke recovery. *Neurology* 2016;87:1407-16.
2. Pollock A, St George B, Fenton M, et al. Top ten research priorities relating to life after stroke. *Lancet Neurol* 2012;11:209.
3. Jeffers MS, Pittman A, Kendzerska T, et al. Self-reported sleep disturbances among people who have had a stroke: a cross-sectional analysis. *CMAJ* 2023;195:E354-62.
4. Johnson KG, Johnson DC. Frequency of sleep apnea in stroke and TIA patients: a meta-analysis. *J Clin Sleep Med* 2010;6:131-7.
5. Kaneko Y, Hajek VE, Zivanovic V, et al. Relationship of sleep apnea to functional capacity and length of hospitalization following stroke. *Sleep* 2003;26:293-7.
6. Boulos MI, Dharmakulaseelan L, Brown DL, et al. Trials in sleep apnea and stroke: learning from the past to direct future approaches. *Stroke* 2021;52:366-72.
7. McEvoy RD, Antic NA, Heeley E, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. *N Engl J Med* 2016;375:919-31.
8. Johnson KG, Johnson DC. When will it be time? Evaluation of OSA in stroke and TIA patients. *Sleep Med* 2019;59:94-5.
9. Brown DL, Jiang X, Li C, et al. Sleep apnea screening is uncommon after stroke. *Sleep Med* 2019;59:90-3.
10. Chan W, Coutts SB, Hanly P. Sleep apnea in patients with transient ischemic attack and minor stroke: opportunity for risk reduction of recurrent stroke? *Stroke* 2010;41:2973-5.
11. Boulos MI, Kamra M, Colelli DR, et al. SLEAP SMART (Sleep Apnea Screening Using Mobile Ambulatory Recorders After TIA/Stroke): a randomized controlled trial. *Stroke* 2022;53:710-8.
12. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014;45:2160-236.
13. Wein T, Lindsay MP, Cote R, et al. Canadian stroke best practice recommendations: Secondary prevention of stroke, sixth edition practice guidelines, update 2017. *Int J Stroke* 2018;13:420-43.
14. Barbé F, Duran-Cantolla J, Sanchez-de-la-Torre M, et al. Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. *JAMA* 2012;307:2161-8.
15. Peker Y, Glantz H, Eulenburg C, et al. Effect of positive airway pressure on cardiovascular outcomes in coronary artery disease patients with nonsleepy obstructive sleep apnea. the RICCADSA randomized controlled trial. *Am J Respir Crit Care Med* 2016;194:613-20.
16. Labarca G, Dreyse J, Drake L, et al. Efficacy of continuous positive airway pressure (CPAP) in the prevention of cardiovascular events in patients with obstructive sleep apnea: systematic review and meta-analysis. *Sleep Med Rev* 2020;52:101312.
17. Baillieul S, Dekkers M, Brill AK, et al. Sleep apnoea and ischaemic stroke: current knowledge and future directions. *Lancet Neurol* 2022;21:78-88.
18. Gottlieb DJ, Punjabi NM. Diagnosis and management of obstructive sleep apnea: a review. *JAMA* 2020;323:1389-400.

Competing interests: Mark Boulos reports funding from the Canadian Institutes of Health Research, Canadian Partnership for Stroke Recovery, Alternative Funding Plan from the Academic Health Sciences Centres of Ontario, Ontario Genomics and McLaughlin Centre for Molecular Medicine. He also reports consulting fees and honoraria from Jazz Pharmaceuticals, Paladin Labs, Eisai and the OntarioMD Peer Leader Program; travel support from McGill University; and receipt of sleep equipment or research support from Braebon Medical Corporation, The Mahaffy Family Research Fund and Green Mountain.

This article was solicited and has not been peer reviewed.

Affiliations: Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre; Department of Medicine, Division of Neurology, University of Toronto; Sunnybrook Sleep Laboratory, Sunnybrook Health Sciences Centre, Toronto, Ont.

Correspondence to: Mark Boulos, mark.boulos@utoronto.ca